Original article

Association of anti dsDNA antibodies titer with non-renal manifestations of Systemic Lupus Erythematosus and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)

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ABSTRACT

Background: Early diagnosis and effective treatment in systemic lupus erythematosus (SLE) has very crucial role. Anti dsDNA is very important diagnostic tool and activity marker in SLE. This study aimed to determine the association of anti dsDNA antibodies titer with non-renal manifestations of systemic lupus erythematosus and systemic lupus erythematosus disease activity index (SLEDAI).

Patients and methods: It was a cross-sectional study and was carried out at Department of Rheumatology and Immunology, Tertiary Care Hospital, Lahore from Feb 2021 to May 2021. The study involved 69 male and female patients satisfying the systemic lupus international collaborating clinics (SLICC) classification criteria. Questions regarding different symptoms were asked and disease activity parameters were noted excluding renal parameters. Anti-dsDNA titers were measured from standard laboratory using immunofluorescence technique and were correlated with SLEDAI score. A written informed consent was obtained from every patient.

Results: The mean age of the patients was 30.7±10.2 years while the mean duration of disease 1.94±2.65 years. We observed a female predominance among these patients with male to female ratio of 1:7.6. There were fifty-four (78.3%) patients with active disease. The mean anti-dsDNA levels were significantly higher in patients with active disease (315.73±481.68 vs. 78.46±113.64 IU/mL; p-value=0.003). There was a significantly strong positive correlation between anti-dsDNA levels and SLEDAI score (r=0.358; p-value=0.006). When compared, significant difference was observed in mean anti-dsDNA titers in patients with chronic cutaneous manifestations (p-value=0.040), lymphopenia (p-value= 0.012), pleurisy/pericarditis (p-value= 0.024) and leukopenia <3000/mm^3 (p-value= 0.001).

Conclusion: Anti-dsDNA antibodies titers are remarkably increased in patients with non-renal manifestations of systemic lupus erythematosus particularly with chronic cutaneous manifestations and leukopenia and positively correlate with disease activity status and SLEDAI score.

Keywords:

Systemic lupus erythematous (SLE), Anti-ds DNA, Systemic lupus erythematosus disease activity index (SLEDAI)

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disorder characterized by production of autoantibodies and multisystem involvement resulting in substantial morbidity, adding economic burden and poor quality of life.[1,2] It also adds to long-term mortality.[2] The exact etiopathogenesis is not yet known, but involves loss of immune tolerance against self-antigen leading to development of autoantibodies.[3] This inadvertent activation of immune system may be triggered by genetic, endocrine and environmental factors.[1,3]

Early diagnosis and effective treatment remains crucial in the management of patients with SLE.[4] Systemic lupus erythematosus disease activity index (SLEDAI) is a routinely used tool to assess the clinical severity of disease and plan the management. A SLEDAI score of ≥6 is usually considered as active disease.[5] Among the various antibodies detectable in patients with SLE, anti-nuclear antibodies are most sensitive with case positivity rates of up to 95% but these are least specific.[6] Antibodies to double stranded DNA (Anti-dsDNA) are detected in only 60-70% of cases but are highly specific for SLE.[2,6] It has been proposed that in addition to their diagnostic role, anti-dsDNA antibodies levels can also be used to assess the severity of clinical disease and follow the response to treatment in patients with both renal and non-renal SLE.[7-9] However, the available research evidence was limited. Moreover, there was no such published

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research in local population which compelled the present study. The purpose of this study was to determine the association of anti dsDNA titers in SLE clinical manifestations without renal involvement and to correlate it with systemic lupus erythematosus disease activity index (SLEDAI).

PATIENTS AND METHODS

This was a cross-sectional study which was carried out at the Department of Rheumatology and Immunology Tertiary Care Hospital, Lahore for period of 3 months from 10-2-2021 to 9-5-2021 after approval by Institutional Review Board. Sample size of 69 patients was calculated with 5% margin of error and 95% confidence interval using expected population proportion of 5.0%[5]. Patients of both genders with ages in the range of 16-70 years satisfying the systemic lupus international collaborating clinics (SLICC) classification criteria were included. Those with proteinuria more than 500mg/24hours and deranged RFTs or any other renal disease were excluded. Questions regarding different symptoms were asked and disease activity parameters were noted excluding renal parameters. Anti-dsDNA titers were measured from standard laboratory using ELISA technique. Disease activity was assessed on SLEDAI and those with SLEDAI score ≥6 were considered to have active disease. Age, duration of disease, anti-dsDNA antibodies levels have been described by mean ±SD while marital status, various non-renal SLE manifestations and active disease have been described by frequency and percentage. Pearson's correlation has been determined for SLEDAI score and anti-dsDNA levels considering $p \leq 0.05$ as significant while independent sample t-test has been applied to compare mean anti-dsDNA levels between patients with versus without active disease and across various extra renal manifestations of SLE considering $p \leq 0.05$ as significant.

RESULTS

The mean age of the patients was 30.7±10.2 years (ranged from 16 to 62 years). We observed a female predominance among these patients with male to female ratio of 1:7.6 and forty (58.0%) patients were married. Duration of disease ranged from 1 to 13 years with a mean of 1.94±2.65 years.

Anti-dsDNA levels ranged from 0.0 to 2400 IU/mL with a mean of 271.9±446.1 IU/mL. Systemic lupus erythematosus disease activity index (SLEDAI) score ranged from 0 to 31 with a mean of 9.43±6.17. There was a significantly strong positive correlation between anti-dsDNA levels and SLEDAI score (r=0.358; p-value=0.006). There were 54 (78.3%) patients with active disease. The mean anti-dsDNA levels were significantly higher in patients with active

Table 1. Correlation between Anti-dsDNA Levels and SLEDAI (n=69)

	Mean ±SD	Spearman's Correlation (r)	p-value
Anti-dsDNA Levels (IU/mL)	271.9±446.1	0.358	0.006*
SLEDAI Score	9.43±6.17		
	Active Disease (SLEDAI≥ 6)		
Anti-dsDNA Levels (IU/mL)	Yes	No	
	315.73±481.68	78.46±113.64	0.003**

* Observed correlation was statistically significant

** Observed difference was statistically significant on independent sample t-test

Table 2. Comparison of anti-dsDNA levels (IU/mL) among non-renal manifestations of SLE over SLICC criteria

Non-Renal Manifestation	Anti-dsDNA Level (IU/mL)		p-value
	Present	Absent	
Acute Cutaneous Manifestations	290.30±506.84	257.35±399.35	0.781
Chronic Cutaneous Manifestations	81.67±98.46	282.06±455.42	0.040*
Oral and Nasal Ulcers	258.35±356.13	282.52±511.19	0.838
Alopecia	258.39±501.09	290.21±367.47	0.789
Arthritis	297.59±499.49	213.29±294.36	0.509
Serositis	464.80±727.60	232.50±363.10	0.135
ANA	235.51±357.99	453.94±775.76	0.175
Anti-sm	193.75±287.81	279.74±463.49	0.614
Anti-phospholipid Antibodies	364.67±160.70	263.20±453.29	0.703
Neurological Symptoms	312.00±587.87	262.50±427.39	0.784
Hemolytic Anemia	421.20±390.83	254.37±448.22	0.425
Leukopenia	674.75±718.35	239.24±411.89	0.057
Lymphopenia	494.41±711.17	178.87±233.09	0.012*
Thrombocytopenia	147.59±208.24	305.00±488.93	0.248
Low C3 and C4 Levels	348.83±536.95	192.91±324.04	0.175
Positive Coombs Test (direct)	520.25±272.94	250.28±449.07	0.242

* Significant difference on independent sample t-test

Table 3. Comparison of Anti-dsDNA Levels (IU/mL) among Non-Renal Manifestations of SLE over SLEDAI criteria

Non-Renal Manifestation	Anti-dsDNA Level (IU/mL)		p-value
	Present	Absent	
Psychosis	174.00±112.48	273.24±453.83	0.709
Organic Brain Syndrome	831.0±1121.47	248.87±411.98	0.067
CVA	140.00±197.99	272.70±449.44	0.681
Vasculitis	271.42±315.54	267.49±472.47	0.978
Arthritis	331.59±524.74	209.05±348.92	0.288
New rash	381.09±595.70	202.96±315.93	0.135
Alopecia	251.81±391.96	277.14±473.11	0.835
Mucosal ulcer	233.89±304.25	284.20±497.19	0.686
Pleurisy/pericarditis	523.75±731.82	204.40±316.80	0.024*
Hypocomplementemia	411.74±571.78	172.63±304.46	0.040*
Increase dsDNA >25% by far assay	393.34±514.32	52.25±92.22	0.003*
Fever >38	365.24±567.85	255.47±429.18	0.542
Thrombocytopenia <100,000	186.95±270.94	297.85±490.42	0.396
Leukopenia <3000	48.00±41.43	297.37±463.94	<0.001*

* Significant difference on independent sample t-test

disease (315.73±481.68 vs. 78.46±113.64 IU/mL; p-value=0.003) as shown in Table 1.

When compared, significant difference was observed in mean anti-dsDNA titers in patients with chronic cutaneous manifestations, lymphopenia, pleurisy/pericarditis and leukopenia <3000/mm^3 as shown in Tables 2 and 3.

DISCUSSION

Diagnosis of SLE might be straight forward but the management of disease is complex due to multisystem involvement comprising renal as well as extra renal manifestations.[1,2] Timely diagnosis and appropriate treatment is the corner stone in determining the overall survival of patients with SLE.[3,4] However, assessment of disease severity and response to treatment has always been challenging where SLEDAI score has been used to predict the course of disease.[5] Recent research has focused on the prognostic significance of anti-dsDNA levels in addition to its conventional role in the diagnostic workup of patients with SLE where a few studied have reported that higher levels of anti-dsDNA correlate with active disease.[7-9] However, due to limited already published research and lack of local such evidence, need for the present study was felt.

In the present study we noted that the mean age of the patients suffering from systemic lupus erythematosus was 30.7±10.2 years and there was female predominance (M:F; 1:7.6).Our observation is in line with that of another local study where Hussain et al[10] (2011) observed a comparable mean age of 30.4±1.7 years and reported a female predominance with male to female ratio of 1:9 among SLE patients at Services Institute of Medical Sciences, Lahore. Ishaq et al.[11] (2013) observed similar mean age of 31.6±10.5 years among SLE patients presenting at Jinnah Medical College Hospital, Karachi with female to male ratio of 16:1. In another local study conducted at Bahawal Victoria Hospital Bahawalpur, Naheed et al[12] (2016) observed similar mean age of 29.9±4.6 years among such patients. They too reported a female predominance with male to female ratio of 1:11.5. Comparable mean age of 31.0±10.0 years has been reported by Ashraf et al[13] (2020) with a male to female ratio of 1:3.1 among SLE patients presenting at Dermatology, Institute of Skin Diseases Sindh Karachi. Our observation is also comparable to that of Mumtaz et al[14] (2017) who reported a similar mean age of 30.9 years among such patients with male to female ratio of 1:24 at Pakistan Institute of Medical Sciences Islamabad. Bharath et al[15] (2019) reported a comparable mean age of 30.6±10.3 years and female predominance with male to female ratio of 1:49 in Indian such patients while Ahmed et al[16] (2019) reported it to be 34.5±9.3 years in Bangladesh. Bartaula et al[17] (2019) reported a comparable mean age of 32 years and male to female ratio of 1:11.5 among SLE patients in Nepal. In a similar study involving Sri Lankan patients with SLE, Herath et al[18] (2017) reported a mean age of 28 years and male to female ratio of 1:8.1 in line with the present study.

We observed that there was a significantly strong positive correlation between anti-dsDNA levels and SLEDAI score with significantly elevated levels among patients with active disease. Our observation is in line with a similar study where Narayanan et al[19] (2010) evaluated Indian patients with SLE and observed a significant positive correlation between anti-dsDNA levels and SLEDAI score (r=0.576; p=0.01). They too reported similar significantly higher levels of anti-dsDNA antibodies among patients with active disease (82.24±92.70 vs. 30.97±15.10 IU/mL; p-value<0.05). In another similar study, Dhason et al[20] (2017) observed similar significant and positive correlation between anti-

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dsDNA titers and systemic lupus erythematosus disease activity index and reported it to be r=0.432 (p-value<0.001). Our observation is also in line with that of Gheita et al[21] (2018) who observed similar significantly higher levels of anti-dsDNA in patients with active disease (133.20±100.50 vs. 22.03±17.20 IU/mL; p-value<0.0001). Contrary to present study they reported elevated Anti-dsDNA antibodies in patients with musculoskeletal disease and antiphospholipid antibodies. While in our study we found significant higher levels with chronic cutaneous manifestations, lymphopenia/leukopenia and Serositis (Pericarditis/ Pleurisy).

To conclude, SLE was frequently diagnosed in younger females. The anti-dsDNA antibodies levels were significantly raised in patients with systemic lupus erythematosus particularly in disease active patients. The titers correlated positively with the disease activity status on SLEDAI score. A higher level among patients with chronic cutaneous manifestations and leukopenia/lymphopenia were observed. The strengths of the present study were its large sample size of 69 cases and strict exclusion criteria. An important limitation to the present study was that we didn't correlate the anti-dsDNA titers to clinical therapy which could have further shed light on its prognostic significance. Such a study will further highlight the role of anti-dsDNA antibodies in formulating the management of SLE patients and is highly recommended in future clinical research.

CONCLUSION

Anti-dsDNA antibodies titers are remarkably increased in patients with non-renal manifestations of systemic lupus erythematosus particularly in chronic cutaneous manifestations, leukopenia and Serositis (Pericarditis/Pleuricy) and positively correlate with SLEDAI score. So we recommend to calculate SLEDAI in every patient coming in OPD for disease activity monitoring.

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